PACKAGING SYSTEM FOR OXYGEN-SENSITIVE DRUGS

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Application Ser. No. 61/785,158, filed Mar. 14, 2013, which is hereby incorporated by reference in its entirety.

BACKGROUND OF THE INVENTION

Oxygen sensitivity in drugs and their formulations is a large concern in pharmaceutical development. Often, the oxygen sensitive drug or formulation requires additional excipients, packaging and/or manufacturing steps for stability enhancement and degradation prevention. Chemical approaches, such as pH control, addition of an antioxidant, and control of components are usually considered first as a means of enhancing stability of oxygen-sensitive solutions. A downside of chemical approaches is added complexity to the formulation and additional research needed for identity, compatibility and toxicity of suitable excipients. Nitrogen gassing of a solution and nitrogen blanketing of a container during and/or after filling of a drug is also commonly used in the pharmaceutical industry. However, the efficiency of this process is limited and leads to a residual oxygen level of a few percent. With this standard manufacturing and filling process, the shelf life of oxygen sensitive products is generally reduced to typically around six months as compared to drugs that are not sensitive to oxygen.

SUMMARY OF THE INVENTION

Provided herein are pharmaceutical packaging system for an injectable oxygen-sensitive drug. In one aspect, the pharmaceutical packaging system comprises a primary packaging container comprising an oxygen-sensitive drug, wherein the primary packaging container has an oxygen permeable component and wherein the primary packaging container is packaged under inert conditions, a hermetically sealed secondary packaging which envelops the primary packaging container, wherein the secondary packaging has very low permeability to oxygen, and an oxygen absorber, wherein the oxygen absorber removes the oxygen present at the time of packaging assembly at a rate of up to 60%, up to 70%, up to 80%, up to 90%, or up to 100% per day in the secondary packaging and up to 60%, up to 70%, up to 80%, up to 90%, or up to 100% per month in the primary packaging container.

In some embodiments of the pharmaceutical packaging system, the primary packaging container is a syringe, cartridge, vial or drug storage container. In certain instances, the primary packaging container is a syringe. In some embodiments, the primary packaging container is plastic or glass. In certain instances, the primary packaging container is glass. In some embodiments, the oxygen permeable component is an oxygen permeable cap. In some embodiments, the oxygen permeable component is rubber or plastic. In some embodiments, the oxygen permeable component is a rubber cap.

In some embodiments of pharmaceutical packaging system, the secondary packaging is a bag or blister packaging. In some embodiments, the secondary packaging comprises an oxygen barrier material selected from the group consisting of high density polyethylene (HDPE), ethylene/vinyl alcohol copolymer (EVOH), polypropylene (PP), polyethylene terephthalate (PET), polyethylene naphthalate (PEN), and polyamide (PA), metalized film, aluminum foil, oxide coated films and combinations thereof. In certain instances, the oxygen barrier material is EVOH. In some embodiments, the secondary packaging material comprises a top and bottom web. In certain instances, the bottom web is a thermoformed blister. In certain instances, the thermoformed blister comprises EVOH. In certain instances, the top web is aluminum foil or an EVOH layer.

In some embodiments of pharmaceutical packaging system, the oxygen absorber is placed inside the secondary packaging. In certain instances, the oxygen absorber is a sachet, pouch, canister, capsule, label, sticker, strip, patch, cartridge or container. In some embodiments, the oxygen absorber is incorporated into the material of the secondary packaging. In some embodiments, the oxygen absorber is a coating or layer that lines the secondary packaging. In some embodiments, the oxygen absorber is selected from the group consisting of reduced iron compounds, catechol, ascorbic acid and analogs thereof, metal ligands, unsaturated hydrocarbons and polyamides. In certain instances, the oxygen absorber is a reduced iron compound.

In some embodiments of pharmaceutical packaging system, the oxygen absorber reduces the oxygen level from the time of packaging assembly to about zero percent in about one to seven days, or one to three days in the secondary packaging and in about one to six months, or one to three months in the primary packaging container. In some embodiments, oxygen absorber reduces the oxygen level from the time of packaging assembly to about zero percent in about one day in the secondary packaging and in about one month in the primary packaging container. In some embodiments, the oxygen levels in the primary and secondary packaging remain at about zero percent after the initial reduction in the primary and secondary packaging for at least one year. In some embodiments, the oxygen levels in the primary and secondary packaging remain at about zero percent after the initial reduction in the primary and secondary packaging for at least three years.

In some embodiments of pharmaceutical packaging system, the oxygen-sensitive drug is selected from the group consisting of morphine, hydromorphone, promethazine, dopamine, epinephrine, norepinephrine, esterified estrogen, ephedrine, pseudoephedrine, acetaminophen, ibuprofen, danofloxacin, erythromycin, penicillin, cyclosporine, methyldopate, cetirizine, diltiazem, verapamil, mexiletine, chlorothiazide, carbamazepine, selegiline, oxybutynin, vitamin A, vitamin B, vitamin C, L-cysteine and L-tryptophan. In certain instances, the oxygen-sensitive drug is morphine. In certain instances, the oxygen-sensitive drug is hydromorphone. In certain instances, the oxygen-sensitive drug is promethazine.

In another aspect, the pharmaceutical packaging system comprises a primary packaging container comprising an oxygen-sensitive drug, wherein the primary packaging container has an oxygen permeable component and wherein the primary packaging container is packaged under inert conditions, a hermetically sealed secondary packaging which envelops the primary packaging container, wherein the secondary packaging has very low permeability to oxygen, and an oxygen absorber, wherein the oxygen absorber, after removal of the oxygen present at the time of packaging assembly, maintains an oxygen level of about zero percent in the secondary packaging and an oxygen level of about zero percent in the primary packaging container for about one year. In some embodiments, the oxygen levels in the primary and secondary packaging remain at about zero percent after the initial reduction in the primary and secondary packaging for at least one year. In some embodiments, the oxygen levels in the primary